This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

I Claim:

1. A method of developing therapeutic agents comprising the steps of:

providing a base sequence of an organism's nucleic acid, said base sequence containing at least a portion of genetic information for a biological component of said organism; and

synthesizing an oligonucleotide, the sequence of which is derived from said base sequence, for hybridization with messenger ribonucleic acid specific for said biological component.

- 2. The method of claim 1 further including the step of: transforming said oligonucleotide into a more stable form to inhibit degradation by said organism.
- 3. The method of claim 1 wherein said more stable form is a phosphotriester form.
- 4. The method of claim 1 wherein said biological component is a protein.
- 5. The method of claim 4 wherein said oligonucleotide is a deoxyribonucleotide.
- 6. The method of claim 1 wherein the nucleic acid is ribonucleic acid.
- 7. The method of claim 6 wherein the ribonucleic acid is messenger ribonucleic acid.

- 8. The method of claim 1 wherein the bas sequence comprises about fourteen or more bases.
- 9. The method of claim 1 wherein the base sequence comprises about twenty—three bases.
- 10. The method of claim 1 wherein the order of said base sequence is determined from ribonucleic acid or deoxyribonucleic acid specific for said biological component prior to synthesizing the oligonucleotide.
- 11. The method of claim 1 wherein the order of said base sequence is determined from messenger ribonucleic acid specific for said biological component prior to synthesizing the oligonucleotide.
- 12. The method of claim 1 wherein the order of said base sequence is determined from the biological component's sequence prior to synthesizing said oligonucleotide.
- 13. The method of claim 1 further comprising the step of:

inserting said oligonucleotide into a plasmid for cloning.

- 14. The method of claim 13 wherein said plasmid is pBR322.
- 15. The method of claim 14 wherein said oligonucleotide is inserted into said plasmid with a linker base sequence.

- 16. Th method of claim 5 wherein said linker sequ nce is GATTCGAATC or CTAAGCTTAG.
- 17. The method of claim 5 wherein the linker is susceptible to partial degradation by Hind III or Alu I restriction nuclease.
- 18. The method of claim 1 wherein the base sequence is synthesized chemically.
- 19. The method of claim 1 further comprising the step of:

 cross-hybridizing the base sequence against nucleic

 acid from at least one source other than said organism, whereby
 the base sequence is more specific to said organism.
- 20. A method of selectively controlling activity of one or more specific biological components in a cell without substantially interferring with the activity of other biological components of said cell, said method comprising the steps of:

forming an oligonucleotide having a base sequence substantially complementary to a portion of messenger ribonucleic acid coding for said biological component; and introducing said oligonucleotide into said cell.

5

- 21. The method of claim 20 wherein said oligonucleotide comprises at least about fourteen bases.
- 22. The method of claim 20 wherein said oligonucleotide comprises about twenty-three bases.

- 23. The method of claim 20 wherein said messenger ribonucleic acid codes for a protein.
- 24. The method of claim 23 wherein said protein is follicle stimulating hormone, which has an alpha chain and beta chain.
- 25. The method of claim 24 wherein the oligonucleotide base sequence comprises:

- 26. The method of claim 20 wherein the oligonucleotide is a deoxyribonucleotide.
- 27. The method of claim 20 wherein said hybridization occurs at about 37°C .
- 28. The method of claim 20 wherein said oligonucleotide is formed through diester bonding.
- 29. The method of claim 20 further comprising the step of:

transforming at least a portion of the oligonucleotide into a more stable form to inhibit degradation in said cell.

30. The method of claim 29 wherein said more stable form is a phosphotriester form.

31. A m thod of inhibiting th inf ction of a host organism by a for ign organism, said m thod comprising the steps of:

isolating a base sequence from said foreign organism's nucleic acid, the base sequence containing at least a portion of genetic information coding for a protein vital to said foreign organism's viability;

synthesizing an oligonucleotide, the order of which is derived from said base sequence to be substantially complementary to messenger ribonucleic acid coding for the protein; and

10

treating said foreign organism with an effective amount of the oligonucleotide to hybridize with a portion of said messenger ribonucleic acid and block translation of said protein, thereby inhibiting the viability of the foreign organism.

32. The method of claim 31 further comprising the step of:

transforming said oligonucleotide into a more stable form to inhibit degradation by said organisms.

- 33. The method of claim 32 wherein said more stable form is a phosphotriester form.
- 34. The method of claim 31 further comprising the steps of:

determining the order of the base sequence prior to synthesizing the oligonucleotide.

35. The method of claim 31 further comprising the step of:

cross-hybridizing the oligonucleotide against messenger ribonucleic acid from at least one organism different from said foreign organism to increase the specifity of the oligonucleotide against said foreign organism.

- 36. The method of claim 35 wherein the cross-hybridization is performed against messenger ribonucleic acid from said host organism.
- 37. The method of claim 31 wherein the nucleic acid is deoxyribonucleic acid or ribonucleic acid.
- 38. The method of claim 31 wherein the oligonucleotide is a deoxyribonucleotide.
- 39. The method of claim 31 wherein the oligonucleotide hybridizes only with a messenger ribonucleic acid unique to said foreign organism.
- 40. An agent for use against a living organism, said agent comprising an oligonucleotide in a stabilized form to inhibit degradation by said living organism and having a nucleotide sequence substantially complementary to a base sequence of at least a portion of messenger ribonucleic acid coding for a protein vital to said organism's viability.
- 41. The agent of claim 40 wherein the oligonucleotide is in a phosphotriester form.

July 25

5

a

42. The agent of claim 40 wherein the oligonucleotide has at least about fourt on has s.

Ä,

43. The agent of claim 40 wherein the oligonucleotide has about twenty-three bases.

44. The agent of claim 40 wherein the oligonucleotide is a deoxyribonucleotide.

bul as 45. An agent for use in controlling synthesis of a protein, said agent comprising an oligonucleotide in a stabilized form to inhibit degradation and having a nucleotide sequence substantially complementary to a base sequence of at least a portion of messenger ribonucleic acid coding for said protein.

a

46. The agent of claim 45 wherein the oligonucleotide has at least about fourteen bases.

د ا

47. The agent of claim 45 wherein the oligonucleotide has about twenty-three bases.

48. The agent of claim 45 wherein the oligonucleotide is a deoxyribonucleotide.

Sul O 49. A therapeutic agent useful in controlling synthesis of a protein from an organism, said agent comprising a stabilized oligonucleotide, the sequence of which is derived from ribonucleic or deoxyribonucleic acid isolated from said organism, wherein said sequence is substantially complementary to a portion of messeng r ribonucleic acid coding for said protein.

50. The agent of claim 49 wherein said oligonucleotide is a doxyribonucleotid

51. The agent of claim 49 wherein said cligonucleotide has at least about fourteen bases.

52. The agent of claim 49 wherein said oligonucleotide has about twenty-three bases.

idd at